

What is claimed is:

1. A composition for decreasing cell proliferation, comprising an antibody, drug or agent
5 which reduces or inhibits peripheral-type benzodiazepine receptors (PBR) function.
2. A composition according to claim 1 wherein said agent is a ribozyme capable of digesting
10 PBR RNA such that PBR protein is reduced or eliminated.
3. A composition according to claim 1 wherein said agent is an antisense oligonucleotide
15 complementary to PBR RNA.
4. A composition according to claim 1 wherein said agent is a PBR antagonist.
- 20 5. A method for inhibiting cell proliferation in a subject comprising administering to a subject a composition according to claim 3, in a pharmaceutically acceptable diluent, in a
25 pharmaceutically acceptable amount, such that PBR function is inhibited and cell proliferation is reduced.
6. A method according to claim 5 wherein
30 said cell proliferation is due to a tumor.
7. A method according to claim 6 wherein said tumor is breast cancer.

8. A method for determining aggressive phenotype of a tumor comprising:

(i) contacting a tumor cell with antibodies which recognize PBR; and

5 (ii) detecting the presence of absence of a complex formed between PBR and antibodies specific for PBR in the nucleus of said tumor cells wherein the presence of a complex in the nucleus indicates the presence of aggressive tumor phenotype.

10

9. A method according to claim 8 wherein said tumor is breast cancer.

15 10. A method for determining aggressive tumor phenotype comprising:

(i) contacting a tumor cell with antibodies which recognize PBR;

(ii) detecting the presence of absence of a complex formed between PBR and antibodies specific for
20 PBR in the nucleus of said tumor cells; and

(iii) comparing the amount of complex formed with an amount of PBR complexed from a normal cell, wherein an increase in complex over normal indicates the presence of an aggressive tumor
25 phenotype.

11. A method according to claim 10 wherein said tumor is breast cancer.

30 12. A diagnostic or prognostic kit comprising antibodies against PBR and ancillary reagents suitable for use in detecting the presence of an aggressive tumor phenotype in a subject according to claim 8.

13. A diagnostic or prognostic kit comprising antibodies against PBR and ancillary reagents suitable for use in detecting the presence of an aggressive tumor phenotype in a subject according to claim 10.

14. A method for diagnosing an aggressive tumor phenotype comprising:

(i) contacting a tumor tissue sample with oligonucleotides which recognize PBR RNA;

(ii) detecting the presence or absence of a duplex formed between PBR RNA in said sample and oligonucleotides specific therefor;

(iii) and comparing it to the amount of duplex formed in a normal tissue sample, wherein an increase in duplex in the suspected tissue over normal indicates the presence of an aggressive tumor phenotype.

15. A diagnostic or prognostic kit comprising oligonucleotides which recognize PBR RNA and ancillary reagents suitable for use in detecting the presence of an aggressive tumor phenotype in a subject according to claim 14.

16. A therapeutic method for the treatment or amelioration of diseases and processes that are mediated by increased cell proliferation comprising the steps of administering to an individual in need of such treatment antibodies, drugs or agents which reduce or eliminate the function of PBR in a pharmaceutically acceptable diluent in a pharmaceutically acceptable amount.

17. A therapeutic method for the treatment
or amelioration of diseases and processes mediated by
increased cell proliferation according to claim 16,
5 wherein said disease is cancer.

18. A method according to claim 17, wherein
said tumor is breast cancer.

10 19. A therapeutic method for the treatment
or amelioration of diseases and processes mediated by
increased cell proliferation according to claim 16,
wherein said agent is a ribozyme specific for PBR RNA.

15 20. A composition for reducing cancer
growth comprising an inhibitor of PBR selected from
the group comprising

- (i) PBR specific antibody;
- (ii) PBR antagonist;
- 20 (iii) PBR antisense oligonucleotide; and
- (iv) a natural or synthetic inhibitor of
PBR.

21. A therapeutic method for the treatment
25 or amelioration of diseases and processes that are
mediated by reduced cell proliferation comprising the
step of increasing PBR by administering PBR in a
pharmaceutically acceptable diluent in a
pharmaceutically acceptable amount such that cell
30 proliferation is increased.

22. A therapeutic method for the treatment
or amelioration of diseases and processes that are
mediated by reduced cell proliferation according to
35 claim 16 wherein said PBR is administered to an

individual in a composition comprising a vector and PBR DNA, such that PBR is produced and cell proliferation is increased.

5 23. A therapeutic method for the treatment or amelioration of diseases and processes that are mediated by reduced cell proliferation according to claim 16, wherein PBR is increased by administering a ligand of PBR.

10 24. An *in vitro* method for testing possible agents or drugs for cell proliferation inhibitory activity said method comprising measuring ability of said agent or drug to decrease PBR activity in an *in vitro* assay.

15 25. An *in vitro* method for testing agents or drugs for cell proliferation inhibitory activity according to claim 24, wherein said drug or agent is an antitumour drug or agent.

20 26. An *in vitro* method for testing possible drugs or agent which promote cell proliferation said method comprising measuring ability of said agent or drug to increase PBR function in an *in vitro* assay.

25 27. A composition for detecting PBR comprising at least one of the following: anti PBR antibody, natural PBR ligand, and synthetic PBR ligand.

30 28. A composition according to claim 27 wherein said synthetic ligand is PK11195.

29. A composition according to claim 28 wherein PK11195 is detectably labeled.

30. A method for detecting the level of PBR
5 in cells using the polymerase chain reaction said method comprising:

- (i) extracting RNA from a sample;
- (ii) reverse transcribing said RNA into cDNA
- (ii) contacting said cDNA with
10 (a) at least four nucleotide triphosphates,
(b) a primer that hybridizes to PBR cDNA,

and

- (c) an enzyme with polynucleotide synthetic activity,
15 under conditions suitable for the hybridization and extension of said first primer by said enzyme, whereby a first DNA product is synthesized with said DNA as a template therefor, such that a duplex molecule is formed;

- 20 (iii) denaturing said duplex to release said first DNA product from said DNA;

- (iv) contacting said first DNA product with a reaction mixture comprising:
25 (a) at least four nucleotide triphosphates,
(b) a second primer that hybridizes to said first DNA, and

- (c) an enzyme with polynucleotide synthetic activity,

- 30 under conditions suitable for the hybridization and extension of said second primer by said enzyme, whereby a second DNA product is synthesized with said first DNA as a template therefor, such that a duplex molecule is formed;

- 35 (v) denaturing said second DNA product from said first DNA product;

(vi) repeating steps iii-vi for a sufficient number of times to achieve linear production of said first and second DNA products;

(vii) fractionating said first and second DNA products generated from said PBR cDNA; and

(viii) comparing the level of PBR cDNA with the level of PBR cDNA from a normal cell; wherein, an increase in PBR level over normal cells indicates an aggressive tumor phenotype.

10

31. A method for determining the aggressive phenotype of a tumor cell detecting PBR RNA in said cell and comparing the level of PBR RNA to the level of PBR RNA from a normal cell wherein an increase over normal in PBR RNA in the tumor cell indicates an aggressive tumor phenotype.

15

32. A cDNA comprising the polynucleotide sequence specified in SEQ ID NO:1 or SEQ ID NO:2 encoding a polypeptide comprising the sequence specified in SEQ ID NO:3.

20

33. A cDNA comprising the polynucleotide according to claim 32 and a vector.

25

34. A cell transformed with the cDNA according to claim 33.

35. A PBR negative cell comprising an inactivated PBR gene.

30

36. The PBR negative cell of claim 35 wherein said cell is R12.